DATA EVALUATION RECORD

1-NAPHTHALENEACETIC ACID, SODIUM SALT
(Na^+ NAA Technical)

STUDY TYPES: **Product Identity and Composition (OCSPP 830.1550)**
Description of Materials Used to Produce the Product (OCSPP 830.1600)
Description of the Production Process (OCSPP 830.1620)
Discussion of Formation of Impurities (OCSPP 830.1670)
Preliminary Analysis (OCSPP 830.1700)
Certified Limits (OCSPP 830.1750)
Enforcement Analytical Method (OCSPP 830.1800)
Physical and Chemical Characteristics (OCSPP 830.6302-830.7950)

MRIDs 487129-01 through 487129-03

Prepared for
Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Summitec Corporation
9724 Kingston Pike, Suite 602
Knoxville, Tennessee 37922

Task Order No. 3-A-173

Primary Reviewer:
Maolian Chen, Ph.D.

Signature: Maolian Chen, ME
Date: MAY 08 2012

Secondary Reviewers:
Dennis Opresko, Ph.D.

Signature:
Date: MAY 08 2012

Robert H. Ross, M.S., Program Manager

Signature: Robert H Ross
Date: MAY 08 2012

Quality Assurance:
Angela M. Edmonds, B.S.

Signature: Angela M. Edmonds
Date: MAY 08 2012

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.
Summitec Corporation for the U.S. Environmental Protection Agency under Contract No. EP-W-11-014

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEE

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

DATE: 08/23/12

SUBJECT: Product Chemistry Review of "Na^+ NAA Technical" TGAI/MUP

FROM: Indira Gairola/ Product Chemistry Team
Technical Review Branch / Registration Division (7505P)

TO: Rossemary Kearns / Tony Kish PM 22
Fungicide Branch / Registration Division (7505P)"

DP BARCODE: 398568
DECISION NO.: 459530
REGISTRATION NO./FILE SYMBOL NO.: 73049-UII
PRODUCT NAME: Na^+ NAA Technical
PC CODE: 056007
REGISTRANT: Valent Biosciences Corporation
USE: Plant growth regulator
FOOD USE: Yes [X] No [ ]
MRID NUMBERS: 487129-01 through -03

INTRODUCTION:

The applicant submitted an application for approval of the new manufacturing use product "Na^+ NAA Technical". In support of the application, the applicant submitted Group A product chemistry data with MRID Nos. 487129-01 through 487129-02 and Group B product chemistry data with MRID No. 487129-03. The CSF (dated 12/02/2011) for the basic formulation was also submitted for the product.
The Primary review was done by Summitec Corporation, 9724 Kingston Pike, Suite 602 Knoxville, Tennessee Task Order No. 3-A-11.
TRB has been asked to determine the acceptability of the product chemistry data and basic CSF.

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SUMMARY OF FINDINGS:

1. Group A guidelines:

830.1550 (product identity & composition)

The active ingredient was adequately described (MRID 487129-01). The nominal concentration of the active ingredient (95.0%, from CSF and Page 4 of the confidential attachment in MRID 487129-01) is close to the average derived from the 5-batch preliminary analysis (95.1%, from Page 4 of the confidential attachment in MRID 487129-01). The nominal concentration (96.0%) of the active ingredient on the product label does not match that (95.0%) on the CSF. The product name (Na+ NAA Technical Powder) on the product label does not match that (Na+ NAA Technical) on the CSF.
Applicant is required to change the label clain to 95.1%, of active ingredient, and to change the label for product name as stated above and CSF to 95.1%

830.1600 (description of materials used to produce the product)

1. The submitted data are upgradable. The information presented did not state the supplier for [redacted] on the CSF, hence it does not meet the data requirements for 40 CFR 158.160. but not on CSF? consult this Review

830.1620 (description of production process)

The submitted data are acceptable. Description of the production process was provided in MRID 487129-01. The information presented meets the data requirements for 40 CFR 158.162.

830.1670 (discussion on the formation of impurities)

The submitted data are acceptable (MRID 487129-01). Potential impurities were identified and quantified as part of the five-batch analysis (MRID 487129-02). The information presented meets the data requirements for 40 CFR 158.167.

830.1700 (preliminary analysis)

The submitted data are acceptable. Results are presented for a five-batch analysis (MRID 487129-02) using HPLC-UV. The nominal concentrations of the A.I. were: 93.8, 95.0, 95.9, 95.2 and 95.7% (average 95.1%, from Page 10 in MRID 487129-02). Certificates of Analysis were provided. The information presented meets the data requirements for 40 CFR 158.170.

830.1750 (certified limits)

The nominal concentration for the A.I. was established based on the average of the values from the five-batch analysis (MRID 487129-02). The certified limits for the AI (Upper limit: 97.9% and Lower limit: 92.1%; from CSF and Page 4 of the confidential attachment in MRID 487129-01) are within EPA's Standard Certified Limits. However, the lower certified limits for the impurities should not be included on the CSF.

830.1800 (enforcement analytical method)

The submitted data are acceptable.The analytical method for quantifying the A.I. is HPLC-UV. The method was validated only for detector linearity and precision (MRID 487129-02). The information presented meets the data requirements for 40 CFR 158.180.

2. Group B guidelines (physical-chemical properties):

The registrant submitted experimental data for melting point, bulk density and water solubility (MRID 487129-03). Only results (no experimental data or references) were provided for color, physical state and pH (MRID 487129-03). No data were submitted for odor, stability to normal and elevated temperatures/metals/metal ions, oxidation/reduction,, flammability, explodability, storage stability, miscibility, corrosion characteristics, UV/visible absorption, dissociation constants, partition coefficient, and vapor pressure. However, the Data Matrix table indicates that data are available for all these endpoints, except for miscibility, viscosity and boiling point that are not applicable.

CONCLUSIONS:

The TRB has reviewed the product chemistry data submitted for Technical MUP (produced by Valent Biosciences Corporation) and has concluded that:

1. The product chemistry data submitted corresponding to guidelines 830.1550 (product identity and composition), 830.1620 (description of the production process), 830.1670 (discussion of the formation of impurities), 830.1700 (preliminary analysis) and 830.1750 (certified limits) are acceptable.

2. The product chemistry data submitted corresponding to guideline 830.1600 (description of materials used to produce the product) are upgradable, applicant did not state the supplier for [redacted] on the CSF.

↳ NOT IN CSF?

The product chemistry data submitted corresponding to guideline 830.1800 (enforcement analytical method) are acceptable

3. The proposed CSF for the basic formulation is not acceptable. The data for pH on the CSF is indicated as "N/A" which is different from that (pH: 9-10 for 5% slurry p 7) given in MRID 487129-03. The lower certified limits for the impurities should not be included on the CSF. In order to be consistent applicant is required to change the label clain to
4. 95.0 %, of active ingredient, and to change the label for product name as stated in summary of findings (Group A 830.1550).

5. The nominal concentration (96.0%) of the active ingredient on the product label does not match that (95.0%) on the CSF. The product name (Na+ NAA Technical Powder) on the product label does not match that (Na+ NAA Technical) on the CSF. Applicant needs to submit a corrected label.

6. The registrant submitted 830 Series group B data for melting point, bulk density and water solubility, and results only (no experimental data or references) for color, physical state and pH (MRID 487129-03). No data were provided for other 830 series group B guidelines (see comments above in Summary of Findings).

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830.1550. Product identity & composition: (MRID No. 487129-01)

Common Name: NAA Sodium salt

Chemical name (CAS): 1-Naphthaleneacetic acid, sodium salt

(IUPAC): 1-Naphthaleneacetic acid, sodium salt

CAS No.: 61-31-4

PC Code No.: 056007

Empirical Formula: $C_{12}H_{10}O_2Na$

Molecular Weight: 208.20 g/mole

Structural Formula:

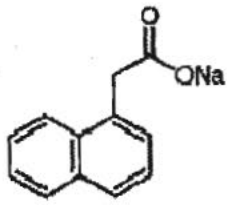

Table 1. Manufacturing and Impurity Data for Technical TGAI "Na^+ NAA Technical."

GLN	Requirement	MRID	Status	Details and/or Deficiency
830.1550	Product Identity & Composition	487129-01	U	Not Adequately described
830.1600	Description of materials used to produce the product	487129-01	U	The local supplier of [redacted] of wes not given.
830.1620	Description of production process	487129-01	A	Description the production process was provided.
830.1670	Discussion on the formation of impurities	487129-01	A	The potential impurities were identified and quantified.
830.1700	Preliminary analysis	487129-02	A	Five-batch analyses of the A.I. by HPLC-UV
830.1750	Certified limits	487129-01	A	The upper and lower certified limits for the A.I. are within EPA's Standard Certified Limits.
830.1800	Enforcement analytical method	487129-01	A	The method for quantifying the A.I.is acceptable.

A = Acceptable; N = Unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress; U = Up-grade (additional information required);

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830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of: Technical TGAI "Na^+ NAA Technical."

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	487129-03	U	White to light tan
830.6303	Physical state	487129-03	U	Solid
830.6304	Odor	405230-03	U	No data provided*
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	405230-03	U	No data provided*
830.6314	Oxidation/reduction: chemical incompatibility	441696-02	U	No data provided*
830.6315	Flammability	CSF (dated 12/02/2011)	NA	Not applicable
830.6316	Explodability	441696-02	U	No data provided*
830.6317	Storage stability	435804-01 441006-02	U	No data provided*
830.6319	Miscibility		G	No data provided*
830.6320	Corrosion characteristics	441006-01 441006-02	U	No data provided*
830.7000	pH	487129-03	U	9-10 (5% slurry) (no experimental data provided)
830.7050	UV/Visible absorption	474786-11	U	No data provided*
830.7100	Viscosity		NA	
830.7200	Melting point	487129-03	A	251 °C
830.7220	Boiling point		NA	
830.7300	Density	487129-03	A	Pour density: 0.298 g/mL Tap density: 0.525 g/mL
830.7370	Dissociation constants in water (DC)	405230-03	U	No data provided
830.7550	Partition coefficient	405230-03	U	No data provided*
830.7840	Water solubility	487129-03	A	324.02 g/L
830.7950	Vapor pressure	405230-03	U	No data provided*

A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress ; U = Up-grade (additional information required); W = waivers

*The Data Matrix table indicates that data are available for all these endpoints (except for miscibility, viscosity and boiling point) and were submitted by a company other than the

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current submitter.

830.1800 (enforcement analytical method)

The analytical method employed to quantify the active ingredient is HPLC-UV. The method was validated for detector linearity and precision, and was not validated for accuracy (MRID 487129-02).

[redacted]

The registrant provided the following information for quantifying the active ingredient (MRID 487129-02).

B. Determination of 1-Naphthylacetic acid sodium by High Pressure Liquid Chromatography (HPLC)

2.B.1 Reference Standard
Name: 1-Naphthylacetic acid PESTANAL®
Lot No.: SZE8112X
Purity: 94.3%
Expiration Date: April 21, 2015
Supplied by: Sigma Aldrich

2.B.2 Method Validation

2.B.2.1. Preparation of Reference Stock Standard Solutions: Approximately 25 mg of the reference standard was weighed into a 25 mL volumetric flask and 20 mL of methanol added. The solution was sonicated for 1 minute and allowed to cool to room temperature before diluting to volume with methanol.

2.B.2.2. Detector Linearity: Detector response linearity was confirmed using a series of five dilutions from the stock standard solution prepared above targeting a range of 0.075 – 0.125 mg/mL. An appropriate amount of the stock standard solution was pipetted

into 10 mL volumetric flasks and diluted to volume with mobile phase (55% MeOH: 45% of 0.5% Acetic Acid (HAc)). Linear regression of the peaks gave a correlation coefficient value of 0.9975 and was considered to be acceptable.

2.B.2.3. Precision: Chromatography of five replicate injections of one sample solution as prepared in 2.B.3.3 produced a relative standard deviation for this study of 0.63%.

2.B.3 Analysis by High Pressure Liquid Chromatography (HPLC)

2.B.3.1. Preparation of Reference Stock Standard Solutions: Stock standard solutions were prepared as previously mentioned in 2.B.2.1.

2.B.3.2. Working Reference Standard Preparation: Appropriate dilutions were made by transferring an appropriate amount of a standard stock solution to 10 mL volume flasks and diluting to volume with mobile phase, mixing well.

2.B.3.3. Test Sample Preparation: Approximately 5 mg aliquots of each batch of the test substance were weighed into separate 50 mL volumetric flasks and 25 mL of mobile phase added. The sample preparations were sonicated for one minute and diluted to volume with mobile phase. Each batch was prepared in triplicate.

2.B.3.4. Analysis: At the beginning of the analysis, the instrument was equilibrated until stable operating conditions were obtained. A solvent blank and two bracketing standards were run; all samples were injected in duplicate.

2.B.3.5. Calculation:

$$\% \text{ AI} = \frac{\text{Calc. Conc.}}{\text{Sample Conc.}} \times \frac{208.2}{186.2} \times 100$$

Where: Calc. Conc. = Sample Peak area/Avg Std Response factor x Purity of Std/100
Avg Std Response Factor = Avg [Std Area/Std Conc (µg/mL)]
Sample Conc (mg/mL) = Sample weight (mg)/Volume of Volumetric flask
208.2 = MW of 1-naphthalene acetic acid, sodium salt
186.2 = MW of 1-naphthalene acetic acid

TABLE 1: HPLC OPERATING CONDITIONS

System	Thermo Finnigan
Column	Zorbax SB-C18 4.6 x 250 mm, 5µm
Column Temperature	35°C
Injection Volume (µL)	5
Detector	UV/Vis
Wavelength (nm)	254
Flow rate (mL/min)	1.0
Run Time (min)	30
Retention time (min)	~ 10.85

Confidential appendix

830.1600 (description of materials used to produce the product)

[redacted]

830.1620 (description of production process)

The registrant provided the following information for this guideline (MRID 487129-01).

Manufacturing process information may be entitled to confidential treatment

Pages 12-14 Manufacturing process information may be entitled to confidential treatment

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830.1700 (preliminary analysis)

[redacted]

830.1750 (certified limits)

The nominal concentration for the active ingredient was established based on the average of the values from the five-batch preliminary analysis (from Page 10 in MRID 487129-02). The certified upper and lower limits of the A.I. are within the range of the guideline OCSPP 830.1750 recommendation.

A copy of the basic CSF dated 12/02/2011 is shown below.

Confidential Statement of Formula may be entitled to confidential treatment